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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,925	09/24/2003	William Hildebrand	6680.055	4622

30589 7590 03/23/2007

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/669,925	HILDEBRAND ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/1/06, 5/25/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,30-51,60-82,91 and 92* is/are pending in the application.

4a) Of the above claim(s) *8-11,18,38-41 and 69-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 12-17, 19-21, 30-37, 42-51, 60-68, 73-82, 91, 92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/30/05, 1/24/05, 9/24/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to Comply with the Sequence Rules.

DETAILED ACTION

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Full compliance with the sequence rules is required in response to this Office Action. A complete response to this Office Action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with both these requirements in the time period set forth in this Office Action will be held non-responsive.

2. Applicant is required under 37 C.F.R. 1.821(d) to amend the specification to list the appropriate SEQ ID NOS for sequences disclosed in the specification (for example, in the Brief Description of the Drawings for Figure 8 and for Figure 15 (*i.e.,* the latter for the two motif peptides disclosed in Figure 15, 9-mer peptides with any amino acid residues at positions 1 and 6-8 and the listed amino acid residues at the motif positions).

3. Applicant's amendment and response filed 12/1/06 and Applicant's amendment filed 5/25/04 are acknowledged and have been entered.

4. Applicant's election of Group I (claims 1-21, 30-51, 62-82 and 92), and species of ELISA plate as the substrate, antibody as the anchoring moiety, W6/32 as the antibody, as well as Applicant's election of the species of HLA-A2 with traverse in Applicant's amendment and response filed 12/1/06 is acknowledged.

Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement for the Group and first three species, the election has been treated as an election without traverse (MPEP 818.03(a)).

The basis for Applicant's traversal of the species election of HLA-A2 is of record in the said amendment and response on page 25, namely that all of the pending claims are generic regarding HLA molecules and the inclusion of this entire genus would not pose an undue search burden on the Examiner.

Applicant's arguments have been fully considered, but are not persuasive.

It is the Examiner's position that there are hundreds of MHC class I and class II molecules, and additionally, the choice of MHC molecule would influence the character of the anchoring molecule in some instances. Therefore, it would be an undue burden on the Examiner to examine the entire genus.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-3, 5-7, 12-17, 19-21, 30-33, 35-37, 42-51, 60-64, 66-68, 73-82, 91 and 92 read on the elected species.

Upon consideration of the prior art, the search has been extended to include the species of magnetic bead and nylon membrane recited in instant claims 4, 34 and 65, and pan-class I or allele-specific antibodies recited in instant claims 7, 37, 51, 68 and 82.

Accordingly, claims 8-11, 18, 38-41 and 69-72 (non-elected species of Group I, and Group II claims) are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-7, 12-17, 19-21, 30-37, 42-51, 60-68, 73-82, 91 and 92 are currently being examined.

5. The amendment filed 5/24/04 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the incorporation by reference to provisional application serial no 60/474,655.

Applicant is required to cancel the new matter in the reply to this Office Action.

6. The abstract of the disclosure is objected to because it does not describe the claimed invention. Correction is required. See MPEP § 608.01(b).

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware of in the specification.

8. The disclosure is objected to because of the following informalities:

a. The use of the trademarks SEPHAROSE, SUPERDEX, CELL-PHARM (misspelled as cell pharm), MACROSEP (including misspelled as macrocep at various places in the specification), LUMINEX and DYNABEADS have been noted in this application, for example at [00070], [00074], [00089], [000102], [00055] and [000120]. They should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

b. The paragraph numbers appear to be incorrect, *i.e.,* for example, [00010] should be [0010].

Appropriate correction(s) is/are required.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 3, 4, 33, 34, 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed an assay or method or kit for detecting the presence of anti-HLA antibodies in a sample *wherein the solid support used in the assay or method or present in the kit is a combination of solid supports such as those recited in the instant claims.*

The instant claims encompass a solid substrate that is more than one type or component of solid substrate.

The specification discloses at ([0120]) "The assay of the presently claimed invention is performed by first attaching sHLA molecules to a substrate, such as a solid support. The substrate may be any insoluble support to which the sHLA molecule can be bound, either directly or indirectly, which is readily separable from soluble material, and which is otherwise compatible with the overall methods of the present invention. The surface of such substrates may be solid or porous, and the substrates may have any shape that allows the substrate to function in accordance with the present invention. Examples of substrates that may be utilized in accordance with the present invention include, but are not limited to, microtiter plates, such as but not limited to ELISA plates; membranes, such as but not limited to, nitrocellulose membranes, PVDF membranes, nylon membranes, acetate derivatives, and combinations thereof; fiber matrix, Sepharose matrix, sugar matrix; plastic chips; glass chips; or any type of bead, such as but not limited to, Luminex beads, Dynabeads, magnetic beads, flow-cytometry beads, and combinations thereof. The substrates are typically formed of glass, plastic or any other type of polymer, such as but not limited to PVC, polyvinyl propylene, polyethylene and the like, polysaccharides, nylon, nitrocellulose, and combinations thereof. Microtiter plates are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. Where separations are made by magnetism, the support generally includes paramagnetic components, preferably surrounded by plastic."

The specification discloses no working examples or description with regards to making or using solid substrates that are combinations or composites of the substrates recited in the instant claims.

The instant disclosure does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera. Since the disclosure fails to provide sufficient relevant identifying characteristics, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

11. Claims 3, 4, 7, 21, 33, 34, 37, 64, 65, 68 and 82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

(a). With regard to the rejection of claims 3, 4, 33, 34, 64 and 65 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement: The specification does not disclose how to make and/or use the instant invention, an assay or method or kit for detecting the presence of anti-HLA antibodies in a sample *wherein the solid support used in the assay or method or present in the kit is a combination of solid supports such as those recited in the instant claims.* The specification has not enabled the breadth of the claimed invention because the claims encompass use of a solid substrate that is more than one type or component of solid substrate. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed assays, method and kits can be made and/or used.

The specification discloses at ([0120]) "The assay of the presently claimed invention is performed by first attaching sHLA molecules to a substrate, such as a solid support. The substrate may be any insoluble support to which the sHLA molecule can be bound, either directly or indirectly, which is readily separable from soluble material, and which is otherwise compatible with the overall methods of the present invention. The surface of such substrates may be solid or porous, and the substrates may have any shape that allows the substrate to function in accordance with the present invention. Examples of substrates that may be utilized in accordance with the present invention include, but are not limited to, microtiter plates, such as but not limited to ELISA plates; membranes, such as but not limited to, nitrocellulose membranes, PVDF membranes, nylon membranes, acetate derivatives, and combinations thereof; fiber matrix, Sepharose matrix, sugar matrix; plastic chips; glass chips; or any type of bead, such as but not limited to, Luminex beads, Dynabeads, magnetic beads, flow-cytometry beads, and combinations thereof. The substrates are typically formed of glass, plastic or any other type of polymer, such as but not limited to PVC, polyvinyl propylene, polyethylene and the like, polysaccharides, nylon, nitrocellulose, and combinations thereof. Microtiter plates are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. Where separations are made by magnetism, the support generally includes paramagnetic components, preferably surrounded by plastic."

The specification discloses no working examples with regards to making or using solid substrates that are combinations or composites of the substrates recited in the instant claims.

Evidentiary reference Zaer *et al* (Transplantation. 1997, 63(1): 48-51, IDS reference) teach that ELISA plates are used alone as a solid support to adsorb HLA complexes to the said support in order to screen for anti-HLA antibodies in patient sera (especially last paragraph at column 2 on page 48).

There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988.

(b). With regard to the rejection of claims 7, 21, 37, 68 and 82 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement (and with regard to the objection of the specification under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure):
Monoclonal antibody W6/32 is critical or essential to the practice of the invention. The reproduction of an identical (hybridoma producing a) monoclonal antibody is an extremely unpredictable event. The monoclonal antibody must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The instant specification does not disclose a repeatable process to obtain the hybridoma that produces W6/32, and it is not apparent if the hybridoma or monoclonal antibody is readily available to the public.

It is noted that the instant specification discloses that "W6/32 is one of the most common monoclonal antibodies (mAb) used to characterize human class I major histocompatibility molecules" ([00081]). It is also noted by the Examiner that said antibody was not invented by Applicant.

Biological materials must be known and readily available to the public (See MPEP 2404.01). Neither concept alone is sufficient. The fact that Applicant and other members of the public were able to obtain the materials in question from a given company does not establish the upon issuance of a patent on the application that such material would continue to be accessible to the public. The Applicant did not make of record any of the facts and circumstances surrounding the access to the biological materials from the company, nor is there sufficient evidence as to the company's policy regarding the material if a patent would be granted.

Even though a hybridoma making the antibody may be commercially available, it does not mean that no restriction is put on the antibody. Further, there is no assurance that the depository would allow unlimited access to the material if the application has matured into a patent.

The Office will accept commercial availability as evidence that a biological material is known and readily available only when the evidence is clear and convincing that the public has access to the material. A product could be commercially available but only at a price that effectively eliminates accessibility to those desiring to obtain a sample. The relationship between the applicant relying on a biological material and the commercial supplier is one factor that would be considered in determining whether the biological material was known and readily available. However, the mere fact that the biological material is commercially available only through the patent holder or the patent holder's agents or assigns shall not, by itself, justify a finding that the necessary material is not readily available, absent reason to believe that access to the biological material would later be improperly restricted.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-7, 12-17, 19-21, 30-37, 42-51, 60-68, 73-82, 91 and 92 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-7, 12-17, 19-21 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: method steps that add a sample to the immobilized HLA molecule on the substrate, separating unbound from bound sample, and detecting the presence of anti-HLA antibodies using a detection system.

Evidentiary reference ALSTEDF teaches that an assay is "A method to analyze or quantify a substance in a sample."

Evidentiary reference ARIUS Research teaches that "Assay means a procedure for the determination of the presence or quantity of a substance."

Evidentiary reference amfar.org teaches that an assay is "A test to detect the presence, absence, or quantity of an agent."

b. Claims 62 and 92 are indefinite in the recitation of "assay" because it is not clear what is meant, *i.e.,* the claims are drawn to a kit, not to a method.

c. Claims 14, 44 and 75 contain the trademark/trade name CELL-PHARM. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is

used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a hollow fiber bioreactor and, accordingly, the identification/description is indefinite.

d. Claims 4, 34 and 65, contain the trademarks/trade names LUMINEX and DYNABEAD[S]. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a hollow fiber bioreactor and, accordingly, the identification/description is indefinite.

e. Claims 1, 5, 6, 12-14, 20, 31, 32, 35, 36, 42-44, 50, 61, 62, 66, 73-75, 81 and 92 are indefinite in the recitation of "individual, soluble HLA molecule" because it is not clear what is meant, *i.e,* if it is just one HLA molecule or multiple copies of one HLA allele product, such as for example, a plurality of HLA-A2 molecules.

f. Claims 14, 44 and 75 are indefinite in the recitation of "inoculating a cell-pharm or a large scale mammalian tissue culture system...such that the cell-pharm produces soluble MHC molecules" because it is not clear what is meant, *i.e.,* if the large scale mammalian tissue culture system also produces soluble MHC molecules.

g. Claims 7, 21, 37, 68 and 82 are indefinite in the recitation of "W6/32" because its characteristics are not known. The use of "W6/32" monoclonal antibody as the sole means of identifying the claimed antibody renders the claim indefinite because "W6/32" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation s to define completely distinct antibodies.

14. For the purpose of prior art rejections, the filing date of the instant claims is deemed to be the filing date of the instant application, *i.e.,* 9/24/03, as the parent applications do not support the claimed limitations of the instant application. The provisional parent application serial no. 60/413,842 only discloses ELISA assays using W6/32 or pan-HLA antibody immobilized HLA to detect anti-HLA antibodies. The provision parent application serial no. 60/474,655 discloses some aspects of making soluble HLA from gDNA or cDNA. The parent application serial no. 10/337,161 and 10/022,066 disclose soluble HLA and making soluble HLA, respectively.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

16. Claims 1-7, 12, 13, 30-37, 42, 43, 60 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,482, 841 (IDS reference).

U.S. Patent No. 5,482, 841 discloses an assay method for detecting the presence of anti-HLA antibodies in a sample, said method comprising extracting HLA molecules from cells and purifying them by mild detergent extraction, centrifugation, and PEG and NH_4SO_4 precipitation, indirectly linking said HLA molecules to a solid support such as beads, membranes and microtiter plates using polyclonal or monoclonal antibodies specific for the α3 domain of Class I HLA or the associated β2m chain or to a conformational epitope expressed by the combination of both chains, or specific to epitopes conserved across a class or subset of HLA molecules, such as ones specific for HLA-A, B or C or ones specific for Class II HLA-DP, DQ or DR. U.S. Patent No. 5,482, 841 further discloses that a sample containing antibodies is added, bound antibodies are separated from free antibodies and other non-specifically bound proteins or other components, and the presence of the antibodies is detected using a labeled reagent such as anti-human antibody against human IgG, IgM or IgA. U.S. Patent No. 5,482, 841 discloses that the samples may be biological fluids such as blood, CSF, tears, saliva, lymph, dialysis fluid, organ or tissue culture derived fluids and fluids extracted from physiological tissues. U.S. Patent No. 5,482, 841 discloses that of particular interest are allo-antibodies found in the serum of transplant or prospective transplant patients, and that the determination of the presence and specificity of antibodies against foreign HLA antigens is therefore clinically important for monitoring transplant patients, and the assay may test for reactivity against a panel of antigens or may be specific for a single donor. U.S. Patent No. 5,482, 841 discloses that the solid support can be microtiter plates (*i.e.,* with wells), glass, plastic, polysaccharides, nylon or nitrocellulose or paramagnetic component materials surrounded by plastic. U.S. Patent No. 5,482, 841 discloses using negative and positive control samples. U.S.

Patent No. 5,482, 841 discloses a kit for use in a method for detecting at least one receptor analyte specific for an HLA antigen in a biological sample, said kit comprising a solid support coated with a capture agent capable of specifically binding to a conserved region of a subset of interest of HLA antigens and a labeled reagent that specifically binds to human antibodies, and wherein the capture agent may be an antibody directed to the α3 domain of HLA class I heavy chain (see entire reference).

With regard to the inclusion of claims 13 and 43 in this rejection, although the art reference does not explicitly disclose that endogenous peptides are present in the binding groove of the extracted HLA molecules, the art reference does disclose that the HLA molecules are purified from membrane bound alloantigens that are mild-detergent-extracted from cells such as leukocytes; therefore, the HLA molecules would be expected to contain a mixture of endogenous peptides in their peptide binding grooves. Therefore, the claimed process appears to be the same as the process of the prior art absent a showing of differences. Since the Patent Office does not have the facilities for examining and comparing the process of the instant invention to those of the prior art, the burden is on Applicant to show a distinction between the process of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

17. Claims 1-7, 12, 13, 30-37, 42, 43, 60 and 61 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,482, 841 (IDS reference).

U.S. Patent No. 5,482, 841 discloses an assay method for detecting the presence of anti-HLA antibodies in a sample, said method comprising extracting HLA molecules from cells and purifying them by mild detergent extraction, centrifugation, and PEG and NH_4SO_4 precipitation, indirectly linking said HLA molecules to a solid support such as beads, membranes and microtiter plates using polyclonal or monoclonal antibodies specific for the α3 domain of Class I HLA or the associated β2m chain or to a conformational epitope expressed by the combination of both chains, or specific to epitopes conserved across a class or subset of HLA molecules, such as ones specific for HLA-A, B or C or ones specific for Class II HLA-DP, DQ or DR. U.S. Patent No. 5,482, 841 further discloses that a sample containing antibodies is added, bound antibodies are separated from free antibodies and other non-specifically bound proteins or other components, and the presence of the antibodies is detected using a labeled reagent such as anti-human antibody against human IgG, IgM or IgA. U.S. Patent No. 5,482, 841 discloses that the samples may be biological fluids such as blood, CSF, tears, saliva, lymph, dialysis fluid, organ or tissue culture derived fluids and fluids extracted from physiological tissues. U.S. Patent No. 5,482, 841 discloses that of particular interest are allo-antibodies found in the serum of transplant or prospective transplant patients, and that the determination of the presence and specificity of antibodies against foreign HLA antigens is therefore clinically important for monitoring transplant patients, and the assay may test for reactivity against a panel of antigens or may be specific for a single donor. U.S. Patent No. 5,482, 841 discloses that the solid

support can be microtiter plates (*i.e.,* with wells), glass, plastic, polysaccharides, nylon or nitrocellulose or paramagnetic component materials surrounded by plastic. U.S. Patent No. 5,482, 841 discloses using negative and positive control samples. U.S. Patent No. 5,482, 841 discloses a kit for use in a method for detecting at least one receptor analyte specific for an HLA antigen in a biological sample, said kit comprising a solid support coated with a capture agent capable of specifically binding to a conserved region of a subset of interest of HLA antigens and a labeled reagent that specifically binds to human antibodies, and wherein the capture agent may be an antibody directed to the α3 domain of HLA class I heavy chain (see entire reference).

With regard to the inclusion of claims 13 and 43 in this rejection, although the art reference does not explicitly disclose that endogenous peptides are present in the binding groove of the extracted HLA molecules, the art reference does disclose that the HLA molecules are purified from membrane bound alloantigens that are mild-detergent-extracted from cells such as leukocytes; therefore, the HLA molecules would be expected to contain a mixture of endogenous peptides in their peptide binding grooves. Therefore, the claimed process appears to be the same as the process of the prior art absent a showing of differences. Since the Patent Office does not have the facilities for examining and comparing the process of the instant invention to those of the prior art, the burden is on Applicant to show a distinction between the process of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. Claims 1-7, 12, 13, 30-37, 42, 43, 60-68, 73-82, 91 and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,482, 841 (IDS reference) in view of U.S. Patent No. 5,292,641 (IDS reference).

U.S. Patent No. 5,482, 841 discloses an assay method for detecting the presence of anti-HLA antibodies in a sample, said method comprising extracting HLA molecules from cells and purifying them by mild detergent extraction, centrifugation, and PEG and NH_4SO_4 precipitation, indirectly linking said HLA molecules to a solid support such as beads, membranes and microtiter plates using polyclonal or monoclonal antibodies specific for the α3 domain of Class I HLA or the associated β2m chain or to a conformational epitope expressed by the combination of both chains, or specific to epitopes conserved across a class or subset of HLA molecules, such as ones specific for HLA-A, B or C or ones specific for Class II HLA-DP, DQ or DR. U.S. Patent No. 5,482, 841 further discloses that a sample containing antibodies is added, bound

antibodies are separated from free antibodies and other non-specifically bound proteins or other components, and the presence of the antibodies is detected using a labeled reagent such as anti-human antibody against human IgG, IgM or IgA. U.S. Patent No. 5,482, 841 discloses that the samples may be biological fluids such as blood, CSF, tears, saliva, lymph, dialysis fluid, organ or tissue culture derived fluids and fluids extracted from physiological tissues. U.S. Patent No. 5,482, 841 discloses that of particular interest are allo-antibodies found in the serum of transplant or prospective transplant patients, and that the determination of the presence and specificity of antibodies against foreign HLA antigens is therefore clinically important for monitoring transplant patients, and the assay may test for reactivity against a panel of antigens or may be specific for a single donor. U.S. Patent No. 5,482, 841 discloses that the solid support can be microtiter plates (*i.e.,* with wells), glass, plastic, polysaccharides, nylon or nitrocellulose or paramagnetic component materials surrounded by plastic. U.S. Patent No. 5,482, 841 discloses using negative and positive control samples. U.S. Patent No. 5,482, 841 discloses a kit for use in a method for detecting at least one receptor analyte specific for an HLA antigen in a biological sample, said kit comprising a solid support coated with a capture agent capable of specifically binding to a conserved region of a subset of interest of HLA antigens and a labeled reagent that specifically binds to human antibodies, and wherein the capture agent may be an antibody directed to the α3 domain of HLA class I heavy chain (see entire reference).

U.S. Patent No. 5,482, 841 does not disclose wherein the kit includes the HLA antigens bound to the support, nor control solutions.

U.S. Patent No. 5,292,641 discloses a kit that includes HLA antigens bound to a solid support, control solutions, and the reagents necessary for the determination of antibodies specific for the HLA antigens (especially column 5 at lines 35-49). U.S. Patent No. 5,292,641 discloses an assay method that utilizes HLA bound to a solid support, said HLA being Class I or Class II or minor histocompatibility antigens and derived from human donors, including from platelets, plasma, serum, lymphoblastoid cell lines, transfectant cell lines, or any other convenient source, said solid support including microtiter plate wells, test tubes, beads, slides, absorbent films, membranes, particles, magnetic particles, glass or plastics. U.S. Patent No. 5,292,641 discloses ELISA techniques and the use of labeled anti-human bodies for detection (see entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the solid substrate comprising an adsorbed anti-HLA capture antibody in the kit disclosed by U.S. Patent No. 5,482, 841 by linking the said capture antibody to the HLA molecule disclosed by both art references, and in particular to the HLA produced from the transfectant cell lines disclosed by U.S. Patent No. 5,292,641, and to have included the control solutions disclosed by U.S. Patent No. 5,292,641 as well as by U.S. Patent No. 5,482, 841 in said kit.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for convenience, by making a test kit already comprising an HLA molecule, *i.e.,* with one HLA molecule bound to the capture agent/solid support because both art references disclose kits used for the same purpose, *i.e.,* detecting anti-human HLA antibodies in patient samples, U.S. Patent No. 5,482, 841 discloses that the assay may test for reactivity against a panel of antigens or may be specific for a single donor, and U.S. Patent No. 5,292,641 discloses that the HLA Class I molecules may be derived from transfected cell lines, *i.e.,* transfected to express a particular HLA molecule. In addition, One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to test for antibodies specific for one or more specific HLA molecules and to have a standardized test kit comprising the said molecules.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included control solutions in the kit disclosed by U.S. Patent No. 5,482, 841, as disclosed for the kit of U.S. Patent No. 5,292,641.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for convenience, because U.S. Patent No. 5,482, 841 teaches the use of negative and positive control samples as does U.S. Patent No. 5,292,641.

With regard to the inclusion of claims 13 and 43 in this rejection, although the art reference does not explicitly disclose that endogenous peptides are present in the binding groove of the extracted HLA molecules, the art reference does disclose that the HLA molecules are purified from membrane bound alloantigens that are mild-detergent-extracted from cells such as leukocytes; therefore, the HLA molecules would be expected to contain a mixture of endogenous peptides in their peptide binding grooves. Therefore, the claimed process appears to be the similar to the process of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the process of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the process of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 62-68, 73-82, 91 and 92 are included in this rejection because the recitation of a method whereby the components of the kit are made carries no patentable weight in these product claims.

20. Claims 1-7, 12, 13, 30-37, 42, 43, 60-68, 73-82, 91 and 92 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,482, 841 (IDS reference) in view of U.S. Patent No. 5,292,641 (IDS reference), Prilliman *et al* (Immunogenetics. 1997, 45: 379-385, IDS reference), DiBrino *et al* (Biochemistry. 1995, 34(32): 10130-10138) and U.S. Patent No. 6,232,445 B1 (IDS reference).

U.S. Patent No. 5,482, 841 discloses an assay method for detecting the presence of anti-HLA antibodies in a sample, said assay comprising HLA molecules extracted from cells and purified by detergent extraction, centrifugation, PEG and NH4SO4 precipitation, said HLA molecules indirectly linked to a solid support such as beads, membranes and microtiter plates by polyclonal or monoclonal antibodies specific for the α3 domain of Class I HLA or the associated β2m chain or to a conformational epitope expressed by the combination of both chains, or specific to epitopes conserved across a class or subset of HLA molecules, such as ones specific for HLA-A, B or C. U.S. Patent No. 5,482, 841 further discloses that a sample containing antibodies is added, bound antibodies are separated from free antibodies and other non-specifically bound proteins or other components, and the presence of the antibodies is detected using a labeled reagent such as anti-human antibody against IgG, IgM or IgA. U.S. Patent No. 5,482, 841 discloses that the samples may be biological fluids such as blood, CSF, tears, saliva, lymph, dialysis fluid, organ or tissue culture derived fluids and fluids extracted from physiological tissues. U.S. Patent No. 5,482, 841 discloses that of particular interest are allo-antibodies found in the serum of transplant or prospective transplant patients, and that the determination of the presence and specificity of antibodies against foreign HLA antigens is therefore clinically important for monitoring transplant patients, and the assay may test for reactivity against a panel of antigens or may be specific for a single donor. U.S. Patent No. 5,482, 841 discloses that the solid support can be microtiter plates (with wells), glass, plastic, polysaccharides, nylon or nitrocellulose or paramagnetic component materials surrounded by plastic. U.S. Patent No. 5,482, 841 discloses using negative and positive control samples. U.S. Patent No. 5,482, 841 discloses a kit for use in a method for detecting at least one receptor analyte specific for an HLA antigen in a biological sample, said kit comprising a solid support coated with a capture agent capable of specifically binding to a conserved region of a subset of interest of HLA antigens and a labeled reagent that specifically binds to human antibodies, and wherein the capture agent may be an antibody directed to the α3 domain of HLA class I heavy chain (see entire reference).

U.S. Patent No. 5,482, 841 does not disclose wherein the kit includes the HLA antigens bound to the support, nor control solutions, nor does U.S. Patent No. 5,482, 841 disclose wherein the assay/method comprises the steps recited in instant claims 14-17, 19, 20, 31-37, 42-51, 60 and 61.

U.S. Patent No. 5,292,641 discloses a kit that includes HLA antigens bound to a solid support, control solutions, and the reagents necessary for the determination of antibodies specific for the HLA antigens (especially column 5 at lines 35-49). U.S. Patent No. 5,292,641 discloses an assay method that utilizes HLA bound to a solid support, said HLA being Class I or Class II or minor histocompatibility antigens and derived from human donors, including from platelets, plasma, serum, lymphoblastoid cell lines, transfectant cell lines, or any other convenient source, said solid support including microtiter plate wells, test tubes, beads, slides, absorbent films, membranes, particles, magnetic particles, glass or plastics. U.S. Patent No. 5,292,641 discloses ELISA techniques and the use of labeled anti-human bodies for detection (see entire reference).

Prilliman *et al* teach large-scale production of Class I HLA in roller bottles (*i.e.,* in a large scale mammalian tissue culture system) for expansion of transfected cells for inoculation into a CELL-PHARM hollow fiber bioreactor for high yield production of Class I HLA. Prilliman *et al* further teach a full-length, single stranded cDNA clone of HLA-B*1501 was used as template in PCR amplification with primers, the 3' primer of which introduces a TGA stop codon, truncating the expressed form of the molecule through removal of the TM and cytoplasmic exons from the coding region. Prilliman *et al* teach the PCR product directionally subcloned into M13, and then subcloned into the mammalian pBJ1-neo expression vector, and the resulting construct transfected into the class I-negative EBVU-transformed lymphoblastoid line 721.221. The said line was grown in a large-scale culture system and the CELL-PHARM bioreactor, the soluble HLA collected, centrifuged, and subjected to affinity purification processing and fractionation (especially materials and methods section).

DiBrino *et al* teach obtaining and amplifying full length cDNA for HLA-B*4403 by PCR amplification of cDNA made from RNA isolated from the human lymphoblastoid B cell line W1B. The cDNA was sequenced, cloned into the expression vector RSV.neo and transfected into Hmy2.C1R cells (class I deficient cell line). DiBrino *et al* teach detection of said HLA using W6/32 monoclonal antibody specific for human Class I molecules. DiBrino *et al* teach HLA-A2 class I HLA molecules (especially materials and methods section).

U.S. Patent No. 6,232,445 B1 discloses that DNA encoding HLA, including HLA class I or class II, may be inserted into a vector with a promoter for expression in eukaryotic cells. U.S. Patent No. 6,232,445 B1 discloses that a variety of standard methods can be used to introduce a DNA segment encoding a desired MHC complex or DNA vector carrying the same into a desired cell, for example, by $CaPO_4$ -mediated transfection or transformation, electroporation or liposome-mediated transfer. U.S. Patent No. 6,232,445 B1 discloses that cells are then cultured under conditions that support the expression of the MHC complex, such as hollow fiber culture systems, roller bottles, bioreactors or fermentors. U.S. Patent No. 6,232,445

B1 discloses that the cells may be mammalian cells (that produce occupied MHC molecules) or other eukaryotic cells such as insect cells, and in the latter instance, a variety of presenting peptides can be loaded or covalently linked to MHC complexes, and the MHC molecules may also be single-chain molecules. U.S. Patent No. 6,232,445 B1 discloses isolating total RNA from a human lymphocyte cell line that expresses an MHC class II gene, generating cDNA by PCR, and using oligonucleotide primers that truncate the extracellular portions of the class II molecule, inserting the truncated PCR product into a vector carrying a promoter, subcloning into an expression vector, including a mammalian expression vector, electroporating mammalian cells to transfect them with a plasmid vector, and selection and large scale production of the HLA molecule, as well as affinity chromatography and fractionation to purify the HLA molecules away from contaminating proteins, including use of antibodies that specifically recognize class I or class II MHC molecules (that produce "empty" MHC molecules) (especially column 28 at lines 28-67, columns 29-32, column 33 at lines 1-6 and Examples).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the solid substrate comprising an adsorbed anti-HLA capture antibody in the kit disclosed by U.S. Patent No. 5,482, 841 by linking the said capture antibody to the HLA molecule disclosed by both art references, and in particular to the HLA produced from the transfectant cell lines disclosed by U.S. Patent No. 5,292,641, and to have included the control solutions disclosed by U.S. Patent No. 5,292,641 as well as by U.S. Patent No. 5,482, 841 in said kit.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for convenience, by making a test kit already comprising an HLA molecule, *i.e.,* with one HLA molecule bound to the capture agent/solid support because both art references disclose kits used for the same purpose, *i.e.,* detecting anti-human HLA antibodies in patient samples, U.S. Patent No. 5,482, 841 discloses that the assay may test for reactivity against a panel of antigens or may be specific for a single donor, and U.S. Patent No. 5,292,641 discloses that the HLA Class I molecules may be derived from transfected cell lines, *i.e.,* transfected to express a particular HLA molecule. In addition, One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to test for antibodies specific for one or more specific HLA molecules and to have a standardized test kit comprising the said molecules.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included control solutions in the kit disclosed by U.S. Patent No. 5,482, 841, as disclosed for the kit of U.S. Patent No. 5,292,641.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for convenience, because U.S. Patent No. 5,482, 841 teaches the use of negative and positive control samples as does U.S. Patent No. 5,292,641.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included in the assay/method the steps of making any HLA molecule of interest such as the HLA molecules taught by Prilliman *et al* and DiBrino *et al* and disclosed by U.S. Patent No. 6,232,445 B1, by isolating mRNA for said HLA molecule, reverse transcribing the mRNA to obtain cDNA, amplifying cDNA by PCR using a primer that truncates after the extracellular region as per the teaching of DiBrino *et al* and as per the disclosure of U.S. Patent No. 6,232,445 B1, inserting the PCR product into a mammalian expression vector, electroporating the plasmid vector into a suitable host cell, and inoculating a CELL-PHARM or other hollow fiber bioreactor or large scale mammalian tissue culture system with said host cell(s), growing said host cells, and harvesting the soluble HLA molecules as per the teaching of Prilliman *et al* and as per the disclosure of U.S. Patent No. 6,232,445 B1, and purifying the HLA molecules as per the teaching of Prilliman *et al* and as disclosed by U.S. Patent No. 6,232,445 B1, including by use of the class I specific antibody W6/32 taught by DiBrino *et al* for production and use of class I HLA molecules, and including the use of W6/32 antibody as a capture agent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to provide a source of HLA molecules for the assay/method for detecting the presence of anti-HLA antibodies in a sample as well as disclosing kits for said use that are disclosed by the combination of Patent No. 5,482, 841 and U.S. Patent No. 5,292,641, since the secondary references Prilliman *et al*, DiBrino *et al*, and U.S. Patent No. 6,232,445 B1 teach or disclose methods of isolating, amplifying and large-scale production of specific HLA class I and class II allele products.

With regard to the inclusion of claims 13 and 43 in this rejection, although the art reference does not explicitly disclose that endogenous peptides are present in the binding groove of the extracted HLA molecules, the art reference does disclose that the HLA molecules are purified from membrane bound alloantigens that are mild-detergent-extracted from cells such as leukocytes; therefore, the HLA molecules would be expected to contain a mixture of endogenous peptides in their peptide binding grooves. Therefore, the claimed process appears to be the similar to the process of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the process of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the process of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 62-68, 73-82, 91 and 92 are included in this rejection because the recitation of a method whereby the components of the kit are made carries no patentable weight in these product claims.

21. Claims 6, 7, 37, 51, 68 and 82 are objected to because of the following informalities: the said claims contain spelling errors, *i.e.,* claim 6 recites "moiety" that should be "moiety", and the remainder of the claims recite "Pan-Class I" that should be "pan-Class I". Appropriate correction is required.

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claims 62-68, 73-82, 91 and 92 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-34, 39-44, 46-52, 54-56, 57-63, 68-73, 75-81 and 83-112 of copending Application No. 10/902,400 in view of U.S. Patent No. 5,482, 841. This is a provisional obviousness-type double patenting rejection.

The kit of the instant claims comprises a detection means for detecting an anti-HLA antibody, whereas the kit of the claims of '400 do not.

U.S. Patent No. 5,482, 841 discloses an assay method for detecting the presence of anti-HLA antibodies in a sample, said method comprising extracting HLA molecules from cells and purifying them by mild detergent extraction, centrifugation, and PEG and NH_4SO_4 precipitation, indirectly linking said HLA molecules to a solid support such as beads, membranes and microtiter plates using polyclonal or monoclonal antibodies specific for the α3 domain of Class I HLA or the associated β2m chain or to a

conformational epitope expressed by the combination of both chains, or specific to epitopes conserved across a class or subset of HLA molecules, such as ones specific for HLA-A, B or C or ones specific for Class II HLA-DP, DQ or DR. U.S. Patent No. 5,482, 841 further discloses that a sample containing antibodies is added, bound antibodies are separated from free antibodies and other non-specifically bound proteins or other components, and the presence of the antibodies is detected using a labeled reagent such as anti-human antibody against human IgG, IgM or IgA. U.S. Patent No. 5,482, 841 discloses that the samples may be biological fluids such as blood, CSF, tears, saliva, lymph, dialysis fluid, organ or tissue culture derived fluids and fluids extracted from physiological tissues. U.S. Patent No. 5,482, 841 discloses that of particular interest are allo-antibodies found in the serum of transplant or prospective transplant patients, and that the determination of the presence and specificity of antibodies against foreign HLA antigens is therefore clinically important for monitoring transplant patients, and the assay may test for reactivity against a panel of antigens or may be specific for a single donor. U.S. Patent No. 5,482, 841 discloses that the solid support can be microtiter plates (*i.e.,* with wells), glass, plastic, polysaccharides, nylon or nitrocellulose or paramagnetic component materials surrounded by plastic. U.S. Patent No. 5,482, 841 discloses using negative and positive control samples. U.S. Patent No. 5,482, 841 discloses a kit for use in a method for detecting at least one receptor analyte specific for an HLA antigen in a biological sample, said kit comprising a solid support coated with a capture agent capable of specifically binding to a conserved region of a subset of interest of HLA antigens and a labeled reagent that specifically binds to human antibodies, and wherein the capture agent may be an antibody directed to the α3 domain of HLA class I heavy chain (see entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have included a detection means in the kit recited in the claims of '400 as per the disclosure of U.S. Patent No. 5,482, 841.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because U.S. Patent No. 5,482, 841 discloses including a detection means in a kit comprising HLA antigens linked to a solid support.

In addition, the steps in the instant claims that recite wherein the HLA is made by isolating mRNA and making cDNA versus those in the claims of '400 that recite isolating gDNA, does not result in a structural difference between the HLA made by each claimed method.

24. No claim is allowed.

25. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
March 9, 2007

CHRISTINA CHAN
PERVISORY PATENT EXAMINER
HNOLOGY CENTER 1600

Notice to Comply	Application No. 10/669,925	Hildebrand and Buchli	
	Examiner Marianne DiBrino	Art Unit 1644	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

(X) 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

(X) 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Applicant is required to provide SEQ ID NO for the sequences disclosed in Figures 8 and 15.

Applicant Must Provide:

☒ An initial ~~or substitute~~ computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial ~~or substitute~~ paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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